******* QUERY RESULTS *******

```
=> d his l39

     (FILE 'HCAPLUS' ENTERED AT 13:36:26 ON 17 MAY 2007)
L39            6 S L37 AND L38

=> d que l39
L7         18084 SEA FILE=HCAPLUS ABB=ON  PLU=ON  9004-61-9/RN OR HYALURONIC
                 ACID
L8         24095 SEA FILE=HCAPLUS ABB=ON  PLU=ON  302-79-4/RN OR RETINOIC ACID
L11        51166 SEA FILE=HCAPLUS ABB=ON  PLU=ON  107-92-6/RN OR BUTYRIC ACID
L13          207 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7 AND (L8 OR L11)
L14        17563 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (MIX?) (2A) (ESTERIF? OR
                 ESTER#)
L15            3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L13 AND L14
L16       897746 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ESTER# OR ESTERIF?
L17           61 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L13 AND L16
L18           61 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L15 OR L17
L19           55 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L18 (L) (THU OR PREP OR IMF
                 OR SPN)/RL
L22         5231 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ESTER? (2A) PARTIAL?
L23            2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L19 AND L22
L24      1424355 SEA FILE=HCAPLUS ABB=ON  PLU=ON  1/SC,SX
L26           18 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L19 AND L24
L27           19 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L23 OR L26
L34           17 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("PERBELLINI A"/AU OR
                 "PERBELLINI ALBERTO"/AU)
L35           46 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("CORADINI D"/AU OR  "CORADINI
                  DANILA"/AU)
L36            7 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L34 AND L35
L37           14 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L27 NOT L36
L38              QUE  ABB=ON  PLU=ON  AY<2003 OR PY<2003 OR PRY<2003 OR MY
                 <2003 OR REVIEW/DT
L39            6 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L37 AND L38


=> d his l54

     (FILE 'MEDLINE, BIOSIS, DRUGU, BIOTECHNO, EMBASE' ENTERED AT 13:45:18 ON
     17 MAY 2007)
L54            8 S L49 OR L53

=> d que l54
L38              QUE  ABB=ON  PLU=ON  AY<2003 OR PY<2003 OR PRY<2003 OR MY
                 <2003 OR REVIEW/DT
L40        36886 SEA HYALURONIC ACID
L41        89306 SEA RETINOIC ACID
L42        36714 SEA BUTYRIC ACID
L43          258 SEA L40 AND (L41 OR L42)
L47       489675 SEA ESTER# OR ESTERIF?
L48           29 SEA L43 AND L47
L49            8 SEA L48 AND L38
L50     16539283 SEA (PREPAR? OR PROCESS OR PROCESSES OR SYNTHE? OR METHOD? OR
                 TECHNI?)
L51          171 SEA L43 AND L50
L52           11 SEA L47 AND L51
L53            1 SEA L52 AND L38
L54            8 SEA L49 OR L53
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=> dup rem l39 l54
FILE 'HCAPLUS' ENTERED AT 14:05:13 ON 17 MAY 2007
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FILE 'EMBASE' ENTERED AT 14:05:13 ON 17 MAY 2007
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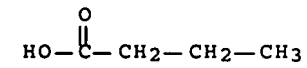
PROCESSING COMPLETED FOR L39
PROCESSING COMPLETED FOR L54
L63           11 DUP REM L39 L54 (3 DUPLICATES REMOVED)
                 ANSWERS '1-6' FROM FILE HCAPLUS
                 ANSWER '7' FROM FILE MEDLINE
                 ANSWER '8' FROM FILE BIOSIS
                 ANSWERS '9-10' FROM FILE DRUGU
                 ANSWER '11' FROM FILE BIOTECHNO

=> d l63 1-6 ibib ed abs hitstr hitind

L63  ANSWER 1 OF 11  HCAPLUS  COPYRIGHT 2007 ACS on STN DUPLICATE 1
ACCESSION NUMBER:         2005:178896  HCAPLUS  Full-text
DOCUMENT NUMBER:          142:384899
TITLE:                    Hyaluronic acid butyric
                          esters in cancer therapy
AUTHOR(S):                Speranza, Annalisa; Pellizzaro, Cinzia; Coradini,
                          Danila
CORPORATE SOURCE:         Unit of Biomolecular Determinants in Prognosis and
                          Therapy, Experimental Department, Istituto Nazionale
                          per lo Studio e la Cura dei Tumori, Milan, Italy
SOURCE:                   Anti-Cancer Drugs (2005), 16(4), 373-379
                          CODEN: ANTDEV; ISSN: 0959-4973
PUBLISHER:                Lippincott Williams & Wilkins
DOCUMENT TYPE:            Journal; General Review
LANGUAGE:                 English
ED   Entered STN:  03 Mar 2005
AB   In this review the authors focus on a promising novel histone deacetylase
     (HDAC) inhibitor (HA-But) obtained by the esterification of butyric acid (BA),
     the smallest HDAC inhibitor, with hyaluronic acid (HA), the main constituent
     of the extracellular matrix which selectively recognizes a transmembrane
     receptor (CD44) overexpressed in most primary cancers and associated with
     tumor progression.  In vitro, HA-But has proved to be 10-fold more effective
     than BA in inhibiting the proliferation of a panel of human cancer cell lines,
     representative of the most common human cancers, and, similar to BA, to
     regulate the expression of some cell cycle-related proteins, to induce growth
     arrest in the G1/G0 phase of the cell cycle and to increase histone
     acetylation.  In vivo, HA-But treatment has demonstrated a marked potency in
     inhibiting primary tumor growth and lung metastases formation from murine
```

Lewis lung carcinoma (LL3) as well as liver metastases formation from intrasplenic implantation of LL3 or B16-F10 murine melanoma cells. In particular, the effect of s.c. and i.p. treatment with HA-But on liver metastases resulted, resp., in 87 and 100% metastases-free animals, and in a significant prolongation of the survival time compared to the control groups. The results suggest that the presence of the HA backbone does not interfere with the biol. activity of butyric residues and that HA-But could represent a promising cell-targetable antineoplastic agent for the treatment of primary and metastatic tumors.

IT **107-92-6, Butyric acid**, biological studies
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**hyaluronic acid** butyric **esters** in cancer therapy)
RN 107-92-6 HCAPLUS
CN Butanoic acid (CA INDEX NAME)



CC **1-0** (Pharmacology)
ST review **hyaluronic acid** butyric **ester** cancer therapy histone deacetylase
IT Antitumor agents
Human
(**hyaluronic acid** butyric **esters** in cancer therapy)
IT **107-92-6, Butyric acid**, biological studies
9004-61-9D, **Hyaluronic acid**, butyric **ester**
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**hyaluronic acid** butyric **esters** in cancer therapy)
IT 9076-57-7, Histone deacetylase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitor; **hyaluronic acid** butyric **esters** in cancer therapy)
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L63 ANSWER 2 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:796308 HCAPLUS Full-text
DOCUMENT NUMBER: 139:286365
TITLE: Methods for preventing and treating loss of balance function due to oxidative stress
INVENTOR(S): Kopke, Richard D.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 16 pp., Cont.-in-part of U.S. Pat. Appl. 2001 7,871.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 2003191064	A1	20031009	US 2003-401682	20030331 <--
US 2001007871	A1	20010712	US 2001-766625	20010123 <--
US 6649621	B2	20031118		

PRIORITY APPLN. INFO.:

US 2001-766625	A2	20010123 <--
US 1997-69761P	P	19971216 <--
US 1998-126707	A2	19980731 <--

ED Entered STN: 10 Oct 2003

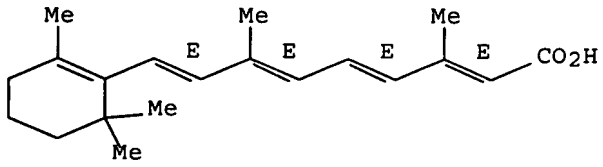
AB The present invention provides methods for preventing and treating loss of, or impairments to, the sense of balance. Specifically, the invention provides methods for preserving the sensory hair cells and neurons of the inner ear vestibular apparatus by preventing or reducing the damaging effects of oxidative stress by administering an effective amount of the following therapeutic agents: antioxidants; compds. utilized by inner ear cells for synthesis of glutathione; antioxidant enzyme inducers; trophic factors; mitochondrial biogenesis factors; and combinations thereof. Acetyl-L-carnitine, D-methionine, and α-lipoic acid prevented loss of inner ear function and hair cell loss in chinchillas stressed with loud noise.

IT **302-79-4, Retinoic acid**
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(antioxidants and other agents for preventing and treating loss of balance function due to oxidative stress)

RN 302-79-4 HCAPLUS

CN Retinoic acid (CA INDEX NAME)

Double bond geometry as shown.



IT **9004-61-9, Hyaluronic acid**
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(as biocompatible carrier; antioxidants and other agents for preventing and treating loss of balance function due to oxidative stress)

RN 9004-61-9 HCAPLUS

CN Hyaluronic acid (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IC ICM A61K038-18
ICS A61K038-06; A61K031-728; A61K031-522; A61K031-426; A61K031-198; A61K031-385; A61K031-05; A61K031-13

INCL 514012000; 514018000; 514161000; 514263310; 514562000; 514440000; 514046000; 514369000; 514645000; 514733000

CC **1-11** (Pharmacology)

IT Fibrins
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(adhesives, as biocompatible carrier; antioxidants and other agents for preventing and treating loss of balance function due to oxidative stress)

IT Enzymes, biological studies
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);

THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antioxidant, inducers of; antioxidants and other agents for preventing and treating loss of balance function due to oxidative stress)

IT Growth factors, animal
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(antioxidants and other agents for preventing and treating loss of balance function due to oxidative stress)

IT Neurotrophic factors
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(brain-derived; antioxidants and other agents for preventing and treating loss of balance function due to oxidative stress)

IT Growth factors, animal
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(epithelial cell growth factors; antioxidants and other agents for preventing and treating loss of balance function due to oxidative stress)

IT Transforming growth factors
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(α-; antioxidants and other agents for preventing and treating loss of balance function due to oxidative stress)

IT 38594-96-6
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(antioxidant enzyme inducer; antioxidants and other agents for preventing and treating loss of balance function due to oxidative stress)

IT 69-72-7, Salicylic acid, biological studies 69-72-7D, Salicylic acid, salts or **esters** 69-93-2, Uric acid, biological studies 501-36-0, Resveratrol 3376-24-7
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(antioxidant; antioxidants and other agents for preventing and treating loss of balance function due to oxidative stress)

IT **302-79-4, Retinoic acid** 61912-98-9, Insulin-like growth factor 67763-96-6, IGF-1 130939-66-1, Neurotrophin-3
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(antioxidants and other agents for preventing and treating loss of balance function due to oxidative stress)

IT **9004-61-9, Hyaluronic acid**
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(as biocompatible carrier; antioxidants and other agents for preventing and treating loss of balance function due to oxidative stress)

IT 3040-38-8, Acetyl-L-carnitine
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(mitochondrial biogenesis factor; antioxidants and other agents for preventing and treating loss of balance function due to oxidative stress)

IT 70-18-8, Glutathione, biological studies
RL: FMU (Formation, unclassified); PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); FORM (Formation, nonpreparative); USES (Uses)
(treatment with compds. used by inner ear cells for synthesis of; antioxidants and other agents for preventing and treating loss of

balance function due to oxidative stress)

IT 63-68-3, L-Methionine, biological studies 70-18-8D, Glutathione, **esters** 348-67-4, D-Methionine 616-91-1, L-N-Acetylcysteine 1200-22-2, α-Lipoic acid 1200-22-2D, α-Lipoic acid, **esters** 19771-63-2 118421-50-4
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); RCT (Reactant); **THU (Therapeutic use)**; BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(used in inner ear cells for synthesis of glutathione; antioxidants and other agents for preventing and treating loss of balance function due to oxidative stress)

L63 ANSWER 3 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:564887 HCAPLUS Full-text
DOCUMENT NUMBER: 135:142255
TITLE: Drug delivery systems for treatment of restenosis and anastomotic intimal hyperplasia
INVENTOR(S): Helmus, Michael N.; Cunanan, Crystal; Tremble, Patrice
PATENT ASSIGNEE(S): Edwards Lifesciences Corporation, USA
SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001054748	A1	20010802	WO 2001-US2563	20010125 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2396628	A1	20010802	CA 2001-2396628	20010125 <--
US 2002026236	A1	20020228	US 2001-771480	20010125 <--
US 6730313	B2	20040504		
EP 1250166	A1	20021023	EP 2001-905081	20010125 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003520830	T	20030708	JP 2001-554731	20010125 <--
AU 775590	B2	20040805	AU 2001-32999	20010125 <--
US 2004202711	A1	20041014	US 2004-816680	20040402 <--
US 6991804	B2	20060131		

PRIORITY APPLN. INFO.:	US 2000-178087P	P	20000125 <--
	US 2001-771480	A1	20010125 <--
	WO 2001-US2563	W	20010125 <--

ED Entered STN: 03 Aug 2001
AB The invention provides methods for treating injuries to 1 or more internal structures of a subject by administering a drug delivery vehicle to an external surface of the injured structure. The drug delivery vehicle substantially adheres to the site of administration and provides for the release of a bioactive agent that reduces or prevents further injury to the internal structure by disease processes, such as hyperplasia. Thus, a fibrin polymer formulation, polymerized from a mixture containing a final concentration of 25-30 mg/mL fibrinogen, 5 IU human factor XIII, 50 IU human

thrombin, and paclitaxel was prepared Also, each vial of paclitaxel formulated in delayed-release microspheres was reconstituted with 4 mL sterile saline, and 2 mL of this mixture was added per vial of a Sealant Protein Concentrate Anal. of the data obtained by angiog. suggested there was no significant difference between control, vehicle and paclitaxel treatment groups.

IT **9004-61-9, Hyaluronic acid**
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(drug delivery systems for treatment of restenosis and anastomotic intimal hyperplasia)
RN 9004-61-9 HCAPLUS
CN Hyaluronic acid (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IC ICM A61L031-16
ICS A61L031-14; A61L031-04; A61L027-22; A61L027-54
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
IT Albumins, biological studies
Antisense oligonucleotides
Corticosteroids, biological studies
Fibronectins
Gelatins, biological studies
Growth factors, animal
Polyamides, biological studies
Polyanhydrides
Polycarbonates, biological studies
Polyesters, biological studies
Polymers, biological studies
Polyoxyalkylenes, biological studies
Polyphosphazenes
Polysaccharides, biological studies
Polyurethanes, biological studies
Taxanes
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(drug delivery systems for treatment of restenosis and anastomotic intimal hyperplasia)
IT Cytokines
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(inhibitors; drug delivery systems for treatment of restenosis and anastomotic intimal hyperplasia)
IT Polyesters, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(lactic acid-based; drug delivery systems for treatment of restenosis and anastomotic intimal hyperplasia)
IT Polyethers, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(ortho **ester** group-containing; drug delivery systems for treatment of restenosis and anastomotic intimal hyperplasia)
IT Polyamides, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(poly(amino acids); drug delivery systems for treatment of restenosis and anastomotic intimal hyperplasia)
IT Polyesters, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(polyamide-; drug delivery systems for treatment of restenosis and anastomotic intimal hyperplasia)
IT Polyamides, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(polyester-; drug delivery systems for treatment of restenosis and

anastomotic intimal hyperplasia)
IT Polyurethanes, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(polyurea-; drug delivery systems for treatment of restenosis and anastomotic intimal hyperplasia)
IT Polyureas
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(polyurethane-; drug delivery systems for treatment of restenosis and anastomotic intimal hyperplasia)
IT Fibrins
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(sealants; drug delivery systems for treatment of restenosis and anastomotic intimal hyperplasia)
IT Proteoglycans, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(sulfated; drug delivery systems for treatment of restenosis and anastomotic intimal hyperplasia)
IT Polyesters, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(thio-; drug delivery systems for treatment of restenosis and anastomotic intimal hyperplasia)
IT Integrins
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(αIIbβ3; drug delivery systems for treatment of restenosis and anastomotic intimal hyperplasia)
IT 33069-62-4, Paclitaxel
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(drug delivery systems for treatment of restenosis and anastomotic intimal hyperplasia)
IT 50-02-2, Dexamethasone 50-02-2D, Dexamethasone, derivs. 107-92-6D, **Butyric acid**, polymers 109-52-4D, Valeric acid, polymers 142-62-1D, Caproic acid, polymers 1605-68-1, Taxane 8001-27-2, Hirudin 8001-27-2D, Hirudin, derivs. 9002-04-4, Thrombin **9004-61-9**, **Hyaluronic acid** 9004-65-3, HPMC 9005-49-6, Heparin, biological studies 9005-49-6D, Heparin, derivs., biological studies 10102-43-9, Nitrogen oxide (NO), biological studies 25322-68-3, Polyethylene glycol 26009-03-0, Poly(glycolic acid) 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] 26100-51-6, Poly(lactic acid) 26124-68-5, Poly(glycolic acid) 55837-20-2, Halofuginone 55837-20-2D, Halofuginone, derivs. 106392-12-5, Pluronic 194554-71-7, Tissue factor inhibitor
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(drug delivery systems for treatment of restenosis and anastomotic intimal hyperplasia)
IT 9054-89-1, superoxide dismutase
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(mimics; drug delivery systems for treatment of restenosis and anastomotic intimal hyperplasia)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L63 ANSWER 4 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:795707 HCAPLUS Full-text
DOCUMENT NUMBER: 132:26876
TITLE: Analgesic and antinociceptive compositions containing polymers
INVENTOR(S): Sessions, Robert W.; Kahn, Alan R.
PATENT ASSIGNEE(S): Ferris Corporation, USA

SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9964081	A1	19991216	WO 1999-US12738	19990607 <--
W: JP, RU				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1085913	A1	20010328	EP 1999-955436	19990607 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6451301	B1	20020917	US 1999-326836	19990607 <--
US 2001009676	A1	20010726	US 2001-789275	20010220 <--
US 6447802	B2	20020910		
US 2002182230	A1	20021205	US 2002-175109	20020619 <--
US 7078055	B2	20060718		
US 2002182173	A1	20021205	US 2002-175119	20020619 <--
US 7078056	B2	20060718		
US 2006210529	A1	20060921	US 2006-440550	20060525 <--
US 2007059251	A1	20070315	US 2006-528780	20060928 <--
US 2007025922	A1	20070201	US 2006-540460	20060929 <--
US 2007025924	A1	20070201	US 2006-541082	20060929 <--
US 2007025925	A1	20070201	US 2006-541153	20060929 <--

PRIORITY APPLN. INFO.:

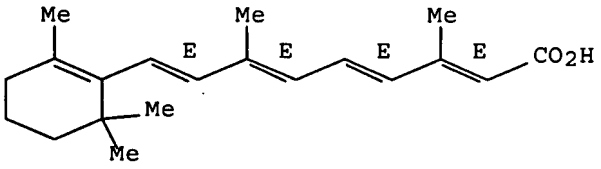
US 1998-88424P	P	19980608 <--
US 1999-326836	A3	19990607 <--
WO 1999-US12738	W	19990607 <--
US 2001-789275	A3	20010220 <--
US 2002-175119	A1	20020619 <--
US 2006-440550	A1	20060525

ED Entered STN: 17 Dec 1999

AB The present invention provides a method of attenuating the response of nociceptors to noxious stimuli by applying a composition comprising a hydrophilic foam substrate, a polymeric hydrophilic agent capable of absorbing water to the surface of the skin. In other aspects, the present invention provides a method of preventing the formation of a bruise in traumatized tissue, a method of attenuating swelling, a method of attenuating neurogenic inflammatory response, and a method of reducing the sensation of pain by applying like compns. to the surface of the skin of patients. A composition comprised a hydrophilic foam substrate, a polymeric hydrophilic agent capable of absorbing water, and a wetting agent to the surface of the skin reduces the sensation of pain and attenuates swelling and bruising. A 65-yr-old male patient underwent arthroscopic surgery to remove a meniscus fragment from his right knee. After the surgery, the knee was dressed with a dressing consisting of Polymem. Following this treatment, the patient required crutches on only one occasion the day of surgery to assist in mobility; the day following the surgery, the patient was able to walk comfortably without orthotics. The patient did not experience significant postoperative pain, and he was not given any pain medication.

IT **302-79-4**, Trans-**Retinoic acid**
9004-61-9, **Hyaluronic acid**
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(analgesic and antinociceptive methods)
RN 302-79-4 HCAPLUS
CN Retinoic acid (CA INDEX NAME)

Double bond geometry as shown.



RN 9004-61-9 HCAPLUS
CN Hyaluronic acid (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IC ICM A61L015-42
ICS A61L015-44
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
IT Alcohols, biological studies
Collagens, biological studies
Gelatins, biological studies
Glycerides, biological studies
Glycols, biological studies
Polymers, biological studies
Polyoxyalkylenes, biological studies
Polysiloxanes, biological studies
Polyurethanes, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(analgesic and antinociceptive methods)
IT Fatty acids, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(ethoxylated; analgesic and antinociceptive methods)
IT Collagens, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(hydrolyzates; analgesic and antinociceptive methods)
IT Alcohols, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(polyhydric; analgesic and antinociceptive methods)
IT 79-10-7D, Acrylic acid, salts, graft copolymers with starch
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(analgesic and antinociceptive compns. containing polymers)
IT 50-03-3, Hydrocortisone acetate 50-70-4, D-Glucitol, biological studies
56-81-5, 1,2,3-Propanetriol, biological studies 57-55-6,
1,2-Propanediol, biological studies 64-17-5, Ethanol, biological studies
67-63-0, 2-Propanol, biological studies 77-99-6 79-06-1D, Acrylamide,
salts, graft copolymers with starch 115-77-5, biological studies
119-36-8, Methyl salicylate **302-79-4**, Trans-**Retinoic**
acid 1490-04-6, Menthol 3068-00-6, 1,2,4-Butanetriol
9000-01-5, Acacia gum 9000-07-1, Carrageenan 9000-30-0, Guar gum
9000-36-6, Karaya gum 9000-69-5, Pectin 9002-18-0, Agar 9003-01-4D,
PolyAcrylic acid, salts **9004-61-9**, **Hyaluronic**
acid 9004-67-5, Methyl cellulose 9005-25-8D, Starch, graft
copolymers with acylates, biological studies 9012-76-4, Chitosan
25322-68-3 25322-69-4, Polypropylene glycol 25618-55-7D, Polyglycerol,
esters 106392-12-5, Polyethylene glycol-polypropylene glycol
block copolymer
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

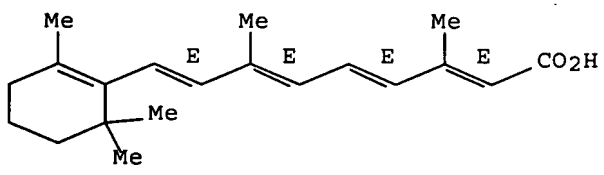
(analgesic and antinociceptive methods)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L63 ANSWER 5 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:267035 HCAPLUS Full-text
DOCUMENT NUMBER: 126:255475
TITLE: Pharmaceutical and cosmetic compositions containing extracts of Foetidia species
INVENTOR(S): Bonte, Frederic; Dumas, Marc; Lavaud, Catherine; Massiot, Georges
PATENT ASSIGNEE(S): Lvmh Recherche, Fr.
SOURCE: Fr. Demande, 20 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2735981	A1	19970103	FR 1995-7707	19950627 <--
FR 2735981	B1	19970919		
WO 9701345	A1	19970116	WO 1996-FR997	19960627 <--

W: JP, US
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
PRIORITY APPLN. INFO.: FR 1995-7707 A 19950627 <--
ED Entered STN: 26 Apr 1997
AB Pharmaceutical and cosmetic compns. containing exts. of Foetidia species are useful for the stimulation of glycosaminoglycans production in the skin and thus moisturizing skin and hair. Methanolic extract of F. africana bark (49 g in 500 mL) was precipitated with acetone, filtered, dialyzed against water and lyophilized to obtain 724 mg lyophilizate rich in saponins. The above extract at a concentration of 10 μg/mL increased the production of glycosaminoglycans by human fibroblasts significantly. A gel contained above extract 0.5, ethanol 5, glycerol 4, Carbopol 940 1.3, and water q.s. 100 g.
IT **302-79-4, Retinoic acid 9004-61-9, Hyaluronic acid**
RL: BUU (Biological use, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(pharmaceutical and cosmetic compns. containing exts. of Foetidia species)
RN 302-79-4 HCAPLUS
CN Retinoic acid (CA INDEX NAME)

Double bond geometry as shown.



RN 9004-61-9 HCAPLUS
CN Hyaluronic acid (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IC ICM A61K035-78
ICS A61K009-10; A61K007-48; A61K007-32; A61K007-025; A61K007-06; A61K007-075
CC 63-4 (Pharmaceuticals)
Section cross-reference(s): 1, 62
IT Steroids, biological studies
RL: BUU (Biological use, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(azasteroids, 4-methyl-4-aza-; pharmaceutical and cosmetic compns. containing exts. of Foetidia species)
IT Alkaloids, biological studies
RL: BUU (Biological use, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(benzylisoquinoline; pharmaceutical and cosmetic compns. containing exts. of Foetidia species)
IT Trace elements, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(pharmaceutical and cosmetic compns. containing exts. of Foetidia species)
IT Glycosaminoglycans, biological studies
Saponins
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BUU (Biological use, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(pharmaceutical and cosmetic compns. containing exts. of Foetidia species)
IT Amino acids, biological studies
Ceramides
Collagens, biological studies
Retinoids
Vitamins
RL: BUU (Biological use, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(pharmaceutical and cosmetic compns. containing exts. of Foetidia species)
IT 9081-34-9, 5α-Reductase
RL: BUU (Biological use, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(inhibitors; pharmaceutical and cosmetic compns. containing exts. of Foetidia species)
IT 50-81-7, Vitamin c, biological studies 51-35-4, Hydroxyproline 56-45-1, Serine, biological studies 56-81-5, Glycerol, biological studies 57-83-0, Progesterone, biological studies 61-90-5, Leucine, biological studies 68-19-9, VITAMINB12 72-19-5, Threonine, biological studies 79-81-2, Retinol palmitate 93-60-7, Methyl nicotinate 116-31-4, Retinaldehyde 123-99-9, Azelaic acid, biological studies 123-99-9D, Azelaic acid, derivs. 127-47-9, Retinol acetate 130-95-0D, Quinine, derivs. 147-85-3, Proline, biological studies **302-79-4**, **Retinoic acid** 302-79-4D, **Retinoic acid, esters** 427-51-0, Cyproterone acetate 464-92-6, Asiatic acid 481-49-2, Cepharanthine 548-40-3, Oxyacanthine 1406-18-4, Vitamin e 7069-42-3, Retinol propionate 7439-95-4, Magnesium, biological studies 7440-50-8, Copper, biological studies 7440-66-6, Zinc, biological studies 7782-49-2, Selenium, biological studies 8059-24-3, Vitamin B6 **9004-61-9**, **Hyaluronic acid** 11032-50-1, Vitamin pp 11103-57-4, Vitamin a 16830-15-2, Asiaticoside 18449-41-7, Madecassic acid 25322-68-3, Peg 34540-22-2, Madecassoside 38304-91-5, Minoxidil 73671-86-0
RL: BUU (Biological use, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

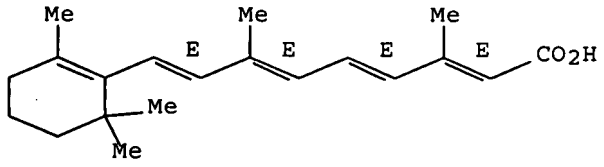
(pharmaceutical and cosmetic compns. containing exts. of Foetidia species)

L63 ANSWER 6 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:456232 HCAPLUS Full-text
DOCUMENT NUMBER: 125:123738
TITLE: Retinoid-based compositions and method for preventing adhesion formation using them
INVENTOR(S): Rodgers, Kathleen E.; Dizerega, Gere S.
PATENT ASSIGNEE(S): University of Southern California, USA
SOURCE: U.S., 13 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5534261	A	19960709	US 1995-373399	19950117 <--

PRIORITY APPLN. INFO.: US 1995-373399 19950117 <--
ED Entered STN: 02 Aug 1996
AB The invention relates to compns. and methods for prevention of adhesion formation, whereby an effective amount of at least one retinoid, e.g., all trans **retinoic acid**, is administered for a period of time sufficient to permit tissue repair. The retinoid is preferably administered in conjunction with a delivery vehicle (e.g., microcapsules, microspheres, biodegradable polymer films, lipid-based delivery systems such as liposomes and lipid foams, viscous instillates and absorbable mech. barriers) useful for maintaining local concns. of the compound at the injury site at an effective level.
IT **302-79-4**, trans-**Retinoic acid**
9004-61-9, **Hyaluronic acid**
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(retinoid-based compns. and method for preventing postoperative adhesion formation using them)
RN 302-79-4 HCAPLUS
CN Retinoic acid (CA INDEX NAME)

Double bond geometry as shown.



RN 9004-61-9 HCAPLUS
CN Hyaluronic acid (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IC ICM A61K009-127
INCL 424450000
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
IT Retinoids
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(retinoid-based compns. and method for preventing postoperative adhesion formation using them)

IT Polyethers, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(ortho ester group-containing, retinoid-based compns. and method for preventing postoperative adhesion formation using them)

IT Acetals
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(poly-, retinoid-based compns. and method for preventing postoperative adhesion formation using them)

IT 9004-34-6, Cellulose, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(oxidized regenerated; retinoid-based compns. and method for preventing postoperative adhesion formation using them)

IT **302-79-4**, trans-**Retinoic acid** 816-94-4, L-α-Distearoylphosphatidylcholine 9004-54-0, Dextran, biological studies **9004-61-9**, **Hyaluronic acid** 9007-28-7, Chondroitin sulfate 9050-04-8, Calcium CM-cellulose 12619-70-4, Cyclodextrin 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] 26202-08-4, Glycolide polymer 26680-10-4, Polylactide 26780-50-7, Lactide-glycolide copolymer 52352-27-9, Polyhydroxybutyric acid 142227-56-3, Lactic acid-glycolide copolymer
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(retinoid-based compns. and method for preventing postoperative adhesion formation using them)

=> d l63 7-11 ibib ab hit ind

L63 ANSWER 7 OF 11 MEDLINE on STN
ACCESSION NUMBER: 2005448216 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 16115366
TITLE: Histone deacetylase inhibitors for treatment of hepatocellular carcinoma.
AUTHOR: Coradini Danila; Speranza Annalisa
CORPORATE SOURCE: UO Tumor Biology and Experimental Therapy, Department of Experimental Oncology, Istituto Nazionale per lo Studio e la Cura dei Tumori, 20133 Milan, Italy.. danila.coradini@istitutotumori.mi.it
SOURCE: Acta pharmacologica Sinica, (2005 Sep) Vol. 26, No. 9, pp. 1025-33. Ref: 84
Journal code: 100956087. ISSN: 1671-4083.
PUB. COUNTRY: China
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200610
ENTRY DATE: Entered STN: 24 Aug 2005
Last Updated on STN: 15 Dec 2005
Entered Medline: 31 Oct 2006

AB Hepatocellular carcinoma (HCC) is one of the most common cancers in the world. Surgical resection has been considered the optimal treatment approach, but only a small proportion of patients are suitable candidates for surgery, and the relapse rate is high. Approaches to prevent recurrence, including chemoembolization before and adjuvant therapy after surgery, have proven to have a limited benefit; liver transplantation is successful in treating limited-stage HCC because only a minority of patients qualify for transplantation. Therefore, new therapeutic strategies are urgently needed. Because in addition to the classical genetic mechanisms of deletion or

inactivating point mutations, epigenetic alterations, such as hyperacetylation of the chromatin-associated histones (responsible for gene silencing), are believed to be involved in the development and progression of HCC, novel compounds endowed with a histone deacetylase (HDAC) inhibitory activity are an attractive therapeutic approach. In particular, pre-clinical results obtained using HA-But, an HDAC inhibitor in which **butyric acid** residues are **esterified** to a **hyaluronic acid** backbone and characterized by a high affinity for the membrane receptor CD44, indicated that this class of compounds may represent a promising approach for hepatocellular carcinoma treatment.

DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)

CT Animals
Antigens, CD44: ME, metabolism
Butyric Acid: PD, pharmacology
***Butyric Acid: TU, therapeutic use**
***Carcinoma, Hepatocellular: DT, drug therapy**
Carcinoma, Hepatocellular: IM, immunology
Carcinoma, Hepatocellular: PA, pathology
Cell Line, Tumor
Cell Proliferation: DE, drug effects
Enzyme Inhibitors: PD, pharmacology
Enzyme Inhibitors: TU, therapeutic use
***Histone Deacetylases: AI, antagonists & inhibitors**
Humans
Hyaluronic Acid: AA, analogs & derivatives
Hyaluronic Acid: PD, pharmacology
***Hyaluronic Acid: TU, therapeutic use**
***Liver Neoplasms: DT, drug therapy**
Liver Neoplasms: IM, immunology
Liver Neoplasms: PA, pathology

RN **107-92-6 (Butyric Acid); 9004-61-9 (Hyaluronic Acid)**

CT Animals
Antigens, CD44: ME, metabolism
Butyric Acid: PD, pharmacology
***Butyric Acid: TU, therapeutic use**
***Carcinoma, Hepatocellular: DT, drug therapy**
Carcinoma, Hepatocellular: IM, immunology
Carcinoma, Hepatocellular: PA, pathology
Cell Line, Tumor
Cell Proliferation: DE, drug effects
Enzyme Inhibitors: PD, pharmacology
Enzyme Inhibitors: TU, therapeutic use
***Histone Deacetylases: AI, antagonists & inhibitors**
Humans
Hyaluronic Acid: AA, analogs & derivatives
Hyaluronic Acid: PD, pharmacology
***Hyaluronic Acid: TU, therapeutic use**
***Liver Neoplasms: DT, drug therapy**
Liver Neoplasms: IM, immunology
Liver Neoplasms: PA, pathology

RN **107-92-6 (Butyric Acid); 9004-61-9 (Hyaluronic Acid)**
CN 0 (Antigens, CD44); 0 (Enzyme Inhibitors); EC 3.5.1.- (Histone Deacetylases)

L63 ANSWER 8 OF 11 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
DUPLICATE 3
ACCESSION NUMBER: 1992:307772 BIOSIS Full-text
DOCUMENT NUMBER: PREV199294020922; BA94:20922
TITLE: STIMULATING EFFECT OF TOCORETINATE ON GRANULATION AND ANGIOGENESIS.

AUTHOR(S): SAKYO K [Reprint author]; ISHIKAWA T; NISHIKI K; OTSUKA N; ITO A; MORI Y
CORPORATE SOURCE: BIOLOGICAL RES LAB, LEDERLE CO LTD, 1-6-34 KASHIWA-CHO, SHIKI, SAITAMA 353, JAPAN
SOURCE: Oyo Yakuri, (1992) Vol. 43, No. 2, pp. 87-95.
CODEN: OYYAA2. ISSN: 0300-8533.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: JAPANESE
ENTRY DATE: Entered STN: 27 Jun 1992
Last Updated on STN: 27 Jun 1992

AB Tocoretinate is the α-tocopherol **ester** of all-trans- **retinoic acid.** The effect of tocoretinate on the formation of granulation tissue was studied. Tocoretinate accelerated the formation of granulation tissue due to cotton pellet in rats in a dose-dependent manner (0.2, 0.5 and 2.0 mg/pellet). At doses equimolar with tocoretinate, **retinoic acid** was equally effective, but α-tocopherol was not. Although the three compounds concerned were used on an equimolar basis, a mixture of **retinoic acid** and α-tocopherol had an effect different from that of tocoretinate. The contents of collagen and glycosaminoglycans (GAGs) increased in the tissues stimulated by tocoretinate. Four GAGs, **hyaluronic acid**, dermatan sulfate, heparan sulfate and chondroitin sulfate, were indentified in both control and tocoretinate-stimulated tissues. In the percentage composition of the GAGs, **hyaluronic acid** was significantly lower but dermatan sulfate was significantly higher in the tocoretinate-stimulated tissues than in the control tissues after 7 days of treatment. Stimulation of granulation by tocoretinate was accompanied with angiogenesis. In vitro, proliferation of rat skin fibroblasts was stimulated by tocoretinate (1 + 10-9 and 1 + 10-8 M). These results suggest that tocoretinate stimulates the formation of granulation tissue through its pharmacological effect of cellular responses.

SO Oyo Yakuri, (1992) Vol. 43, No. 2, pp. 87-95.
CODEN: OYYAA2. ISSN: 0300-8533.

CC Cytology - Animal 02506
Biochemistry studies - Vitamins 10063
Biochemistry studies - Proteins, peptides and amino acids 10064
Biochemistry studies - Lipids 10066
Biochemistry studies - Carbohydrates 10068
Metabolism - Carbohydrates 13004
Metabolism - Proteins, peptides and amino acids 13012
Cardiovascular system - Physiology and biochemistry 14504
Bones, joints, fasciae, connective and adipose tissue - Physiology and biochemistry 18004
Integumentary system - Physiology and biochemistry 18504
Pharmacology - Drug metabolism and metabolic stimulators 22003
Pharmacology - Cardiovascular system 22010
Pharmacology - Connective tissue, bone and collagen-acting drugs 22012
Pharmacology - Integumentary system, dental and oral biology 22020
In vitro cellular and subcellular studies 32600

IT Major Concepts
Cardiovascular System (Transport and Circulation); Cell Biology; Integumentary System (Chemical Coordination and Homeostasis); Metabolism; Pharmacology; Skeletal System (Movement and Support)

IT Miscellaneous Descriptors
RAT SKIN FIBROBLASTS COLLAGEN GLYCOSAMINOGLYCAN

ORGN Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Taxa Notes

Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

L63 ANSWER 9 OF 11 DRUGU COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 1998-37216 DRUGU P G Full-text
TITLE: Improvement of the antiproliferative activity of sodium butyrate by **esterification** with **hyaluronic acid.**
AUTHOR: Coradini D; Pellizaro C; Khan R; Konoewicz P A; Miglierini G; Di Fronzo G
LOCATION: Milan; Trieste, It.
SOURCE: Proc.Am.Assoc.Cancer Res. (39, 89 Meet., 108, 1998) ISSN: 0197-016X
AVAIL. OF DOC.: Oncologia Sperimentale C, Istituto Nazionale per lo Studio e la Cura dei Tumori, Milano, Italy.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB In order to increase the avialability of **butyric acid** over a longer period of time and prolong the biological effect, the Authors covalently linked **butyric acid** with **hyaluronic acid**, whose main advantaged as a drug carrier were the high biocompatibility and the capability to bind to CD44, a specific membrane receptor frequently expressed on tumor cell surface. The incorporation of butyrate residue groups ranged from 15 to 40% of the repeating disaccharide units. After 6 days of treatment, all the **esters** exerted a dose-dependent inhibitory effect and a progressive improvement of the antiproliferative activity, possibly related to the increase in the degree of substitution of the **hyaluronic acid** molecule. When the molecular weight was constant, the highest antiproliferative activity was obtained with 20% of butyrate residues linked. (conference abstract). (No EX).
PY **1998**
AN 1998-37216 DRUGU P G Full-text
P Pharmacology
G Galenics
29 Pharmaceutics
52 Chemotherapy - non-clinical
CT DRUG-DELIVERY *FT; IN-VITRO *FT
[01] BUTYRATE *PH; BUTYRATE *OC; BUTYRATE *RN; ANTIPROLIFERATIVE *FT; PH *FT; OC *FT
[02] HYALURONATE *OC; HYALURONA *RN; AUXILIARY-INGREDIENT *FT; PENETRATION-ENHANCER *FT; PHARMACEUTICS *FT; ANGIOGENESIS-INHIBITORS *FT; OC *FT
RN: 9004-61-9

L63 ANSWER 10 OF 11 DRUGU COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 1986-42148 DRUGU P B V Full-text
TITLE: **Synthesis** of Cellular and Extracellular Glycoproteins by Cultured Human Keratinocytes and Their Response to Retinoids.
AUTHOR: King I A; Pope F M
LOCATION: Harrow, United Kingdom
SOURCE: Biochim.Biophys.Acta C (887, No. 3, 263-74, 1986) 6 Fig. 2 Tab. 56 Ref. ISSN: 0167-4889
AVAIL. OF DOC.: Dermatology Research Group, MRC Clinical Research Centre, Watford Road, Harrow, HA1 3UJ, Middlesex, England.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature

AB Treatment of keratinocyte cultures depleted of vitamin A with either all-trans **retinoic acid** (ATRA, Sigma-Chemical) or arotinoid ethyl **ester** (AEE, Roche), increased **synthesis** of glycoprotein and glycosaminoglycan components of the extracellular matrix. It appeared that the retinoids selected for populations that **synthesized** large amounts of glycosaminoglycan, fibronectin and other extracellular glycoproteins.

PY **1986**

ABEX **Methods** Keratinocytes derived from human foreskins were grown in vitamin A-depleted medium with or without the addition of ATRA (10 nM-10 uM) or AEE (1 nM-1 uM). Metabolites were labeled with 3H-glucosamine, 3H-leucine or 35S-methionine and identified by SDS-polyacrylamide gel electrophoresis (PAGE) and immunoblotting. Results Keratinocytes labeled with 3H-leucine and 95% of the label in the cell layer; on labeling with 3H-glucosamine, 21% of the labeled macromolecules were in the medium. The major 3H-glucosamine-labeled band contained **hyaluronic acid.** Labeling of extracellular material was similar whether 3H-glucosamine or 3H-leucine was used. Human dermal fibroblasts, human melanocytes and 3T3 feeder cells all showed more 3H-glucosamine-labeled macromolecules than did keratinocytes. Each cell type had a distinctive profile by SDS-PAGE. Cells treated with either retinoid were morphologically distinct from vitamin A-depleted or normal cultures. Protein was reduced by retinoid retreatment and keratinization was inhibited. Label in cell macromolecules were decreased and label in medium increased. Total **synthesis** of keratinocyte fibronectin was increased by retinoid treatment. 35S-Methionine-labeled fibronection was also increased by retinoid treatment. (W91/BJ)

AN 1986-42148 DRUGU P B V Full-text
P Pharmacology
B Biochemistry
V Vitamins
22 Endogenous Compounds
36 Dermatological
42 Vitamins

CT TISSUE-CULTURE *FT; IN-VITRO *FT; SKIN *FT; HUMAN *FT; KERATINOCYTE *FT; PROTEIN-METAB. *FT; GLYCOPROTEIN *FT; GLYCOSAMINOGLYCAN *FT; FIBRONECTIN *FT; INTRACELL. *FT; EXTRACELL. *FT; BIOSYNTH. *FT; MATRIX *FT
[01] TRETINOIN *PH; SIGMA-CHEM. *FT; KERATOLYTICS *FT; VITAMINS-A *FT; ORNITHINE-DECARBOXYLASE-INHIBITORS *FT; TRETINOIN *RN; PH *FT
[02] AROTENOID *PH; ROCHE *FT; CYTOSTATICS *FT; VITAMINS-A *FT; ORNITHINE-DECARBOXYLASE-INHIBITORS *FT; AROTENOID *RN; PH *FT

L63 ANSWER 11 OF 11 BIOTECHNO COPYRIGHT 2007 Elsevier Science B.V. on STN DUPLICATE

ACCESSION NUMBER:	1999:29165200 BIOTECHNO Full-text
TITLE:	**Hyaluronic acid** as drug delivery for sodium butyrate: Improvement of the anti-proliferative activity on a breast-cancer cell line
AUTHOR:	Coradini D.; Pellizzaro C.; Miglierini G.; Daidone M.G.; Perbellini A.
CORPORATE SOURCE:	D. Coradini, Oncologia Sperimentale C, Istituto Nazionale Tumori, Via Venezian 1, 20133 Milan, Italy. E-mail: coradini@istitutotumori.mi.it
SOURCE:	International Journal of Cancer, (**1999**), 81/3 (411-416), 27 reference(s) CODEN: IJCNAW ISSN: 0020-7136
DOCUMENT TYPE:	Journal; Article
COUNTRY:	United States
LANGUAGE:	English

SUMMARY LANGUAGE: English

AB The potential clinical utility of sodium butyrate, a natural compound known to inhibit tumor-cell growth, is hampered by the difficulty of achieving effective in-vivo concentrations. The short half-life (about 5 minutes) of sodium butyrate results in rapid metabolism and excretion. To increase the availability of sodium butyrate over a longer period of time, we co-valently linked it to **hyaluronic acid** (a component of the extracellular matrix). Its major advantages as a drug carrier consist in its high biocompatibility and its ability to bind CD44, a specific membrane receptor frequently overexpressed on the tumor-cell surface. The degree of substitution of **hyaluronic acid** with butyrate residues ranged from d.s. = 0.10 to d.s. = 2.24 (1.8-28.4% w/w). The biological activity of **hyaluronic- acid-butyric-ester** derivatives was evaluated in terms of the inhibition of the growth of the MCF7 cell line and compared with that of sodium butyrate. After 6 days of treatment, we observed a progressive improvement of the anti- proliferative activity up to d.s. = 0.20; thereafter, the anti-proliferative effect of the **ester** derivatives decreased. Fluorescence microscopy showed that after 2 hr of treatment fluorescein-labelled compounds appeared to be almost completely internalized into MCF7 cells, expressing CD44 standard and variant isoforms. These findings indicate that **hyaluronic acid** could offer an important advantage in drug delivery, in addition to its biocompatibility: the ability to bind to CD44, which are known to be frequently over-expressed on the tumor-cell surface.

CT ***butyric acid; *hyaluronic acid;**
*drug delivery system; *breast cancer; hermes antigen; matrigel; cancer cell; gene overexpression; cell growth; growth inhibition; drug half life; extracellular matrix; fluorescence microscopy; flow cytometry; human; human cell; article; priority journal

RN (**butyric acid**) 107-92-6, 156-54-7, 461-55-2; (**hyaluronic acid**) 31799-91-4, 9004-61-9, 9067-32-7; (matrigel) 119978-18-6

AN 1999:29165200 BIOTECHNO Full-text

CT ***butyric acid; *hyaluronic acid;**
*drug delivery system; *breast cancer; hermes antigen; matrigel; cancer cell; gene overexpression; cell growth; growth inhibition; drug half life; extracellular matrix; fluorescence microscopy; flow cytometry; human; human cell; article; priority journal

RN (**butyric acid**) 107-92-6, 156-54-7, 461-55-2; (**hyaluronic acid**) 31799-91-4, 9004-61-9, 9067-32-7; (matrigel) 119978-18-6

******* INVENTOR RESULTS *******

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=> d his l62

     (FILE 'HCAPLUS' ENTERED AT 13:59:37 ON 17 MAY 2007)
L62            8 S L61 OR L36

=> d que l62
L34           17 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("PERBELLINI A"/AU OR
                 "PERBELLINI ALBERTO"/AU)
L35           46 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("CORADINI D"/AU OR  "CORADINI
                  DANILA"/AU)
L36            7 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L34 AND L35
L59          159 SEA FILE=HCAPLUS ABB=ON  PLU=ON  SINTOFARM?/CO,PA,CS
L60           56 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L34 OR L35
L61            3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L59 AND L60
L62            8 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L61 OR L36


=> d his l58

     (FILE 'MEDLINE, BIOSIS, DRUGU, BIOTECHNO, EMBASE' ENTERED AT 13:45:18 ON
     17 MAY 2007)
L58           14 S L57 NOT L54

=> d que l58
L38                QUE  ABB=ON  PLU=ON  AY<2003 OR PY<2003 OR PRY<2003 OR MY
                   <2003 OR REVIEW/DT
L40        36886 SEA HYALURONIC ACID
L41        89306 SEA RETINOIC ACID
L42        36714 SEA BUTYRIC ACID
L43          258 SEA L40 AND (L41 OR L42)
L47       489675 SEA ESTER# OR ESTERIF?
L48           29 SEA L43 AND L47
L49            8 SEA L48 AND L38
L50     16539283 SEA (PREPAR? OR PROCESS OR PROCESSES OR SYNTHE? OR METHOD? OR
                   TECHNI?)
L51          171 SEA L43 AND L50
L52           11 SEA L47 AND L51
L53            1 SEA L52 AND L38
L54            8 SEA L49 OR L53
L55          183 SEA PERBELLINI A?/AU
L56          301 SEA CORADINI D?/AU
L57           16 SEA L55 AND L56
L58           14 SEA L57 NOT L54


=> dup rem l62 l58
PROCESSING COMPLETED FOR L62
PROCESSING COMPLETED FOR L58
L64           11 DUP REM L62 L58 (11 DUPLICATES REMOVED)
                 ANSWERS '1-8' FROM FILE HCAPLUS
                 ANSWERS '9-10' FROM FILE BIOSIS
                 ANSWER '11' FROM FILE DRUGU

=> d l64 1-8 ibib ed abs

L64  ANSWER 1 OF 11  HCAPLUS  COPYRIGHT 2007 ACS on STN DUPLICATE 1
ACCESSION NUMBER:         2006:377288  HCAPLUS  Full-text
```

DOCUMENT NUMBER: 145:369313
TITLE: A novel retinoic/butyric hyaluronan ester for the treatment of acute promyelocytic leukemia: preliminary preclinical results
AUTHOR(S): **Coradini, D.**; Pellizzaro, C.; Scarlata, I.; Zorzet, S.; Garrovo, C.; Abolafio, G.; Speranza, A.; Fedeli, M.; Cantoni, S.; Sava, G.; Daidone, M. G.; **Perbellini, A.**
CORPORATE SOURCE: Experimental Department, Unit of Tumor Biology and Experimental Therapy, Istituto Nazionale per lo Studio e la Cura dei Tumori, Milan, Italy
SOURCE: Leukemia (2006), 20(5), 785-792
CODEN: LEUKED; ISSN: 0887-6924
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 26 Apr 2006
AB All-trans retinoic acid (ATRA) represents the therapy of choice for patients with acute promyelocytic leukemia (APL). However, patients often relapse due to ATRA-resistance. The mol. basis of APL alterations indicates that addition of a histone deacetylase inhibitor to ATRA may restore the sensitivity to retinoids. We explored the in vitro and in vivo effects of a novel retinoic/butyric hyaluronan ester (HBR) on a retinoic acid (RA)-sensitive human myeloid cell line, NB4, and on its RA-resistant subclone, NB4.007/6. In vitro, HBR induced growth arrest and terminal differentiation in RA-sensitive NB4 cells (as confirmed by an increased expression of CD11 family members and nitroblue tetrazolium assay), whereas it inhibited the growth of RA-resistant cells by apoptosis, paralleled by an increase in the levels of caspase 3 and 7. In vivo, HBR treatment of NB4-inoculated severe combined immunodeficient mice resulted in a statistically significant increase in survival time ($P<0.0001$), comparable to that induced by a maximum tolerated dose of RA alone. Also on P388-inoculated mice, HBR was active in contrast to RA that was completely ineffective. Present findings suggest that, owing to the simultaneous presence of RA and an histone deacetylases inhibitor, HBR might be useful in controlling the proliferation of RA-resistant cells and the differentiation of RA-sensitive cells.
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L64 ANSWER 2 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2004:583316 HCAPLUS Full-text
DOCUMENT NUMBER: 142:147954
TITLE: Inhibition of hepatocellular carcinomas in vitro and hepatic metastases in vivo in mice by the histone deacetylase inhibitor HA-But
AUTHOR(S): **Coradini, Danila**; Zorzet, Sonia; Rossin, Raffaella; Scarlata, Ignazio; Pellizzaro, Cinzia; Turrin, Claudia; Bello, Michele; Cantoni, Silvia; Speranza, Annalisa; Sava, Gianni; Mazzi, Ulderico; **Perbellini, Alberto**
CORPORATE SOURCE: Unit of Biomolecular Determinants in Prognosis and Therapy, Experimental Department, Istituto Nazionale per lo Studio e la Cura dei Tumori, Milan, Italy
SOURCE: Clinical Cancer Research (2004), 10(14), 4822-4830
CODEN: CCREF4; ISSN: 1078-0432
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 22 Jul 2004

AB The purpose is to evaluate the CD44-mediated cellular targeting of HA-But, a hyaluronic acid esterified with butyric acid (But) residues, to hepatocellular carcinoma cell lines in vitro and to hepatic tumor metastases in vivo. In vitro, the CD44-dependent cytotoxicity in two human hepatocellular carcinoma cell lines (HepB3 and HepG2) with high and low CD44 expression was investigated; in vivo, the effect on liver metastases originating from intrasplenic implants of Lewis lung carcinoma (LL3) or B16-F10 melanoma in mice was compared with the pharmacokinetics of organ and tissue distribution using different routes of administration. HepB3 and HepG2 cell lines showed different expression of CD44 (78 and 18%, resp.), which resulted in a CD44-dependent HA-But inhibitory effect as demonstrated also by the uptake anal. performed using radiolabeled HA-But (99mTc-HA-But). Pharmacokinetic studies showed different rates of 99mTc-HA-But distribution according to the route of administration (i.v., i.p., or s.c.): very fast (a few minutes) after i.v. treatment, with substantial accumulation in the liver and spleen; relatively slow after i.p. or s.c. treatment, with marked persistence of the drug at the site of injection. The effect of s.c. and i.p. treatment with HA-But on liver metastases originating from intrasplenic implants of LL3 carcinoma or B16-F10 melanoma (both CD44-pos.: 68 and 87%, resp.), resulted in 87 and 100% metastases-free animals, resp. (regardless of the route of administration), and a significant prolongation of the life expectancy compared with control groups. HA-But tends to concentrate in the liver and spleen and appears to be a promising new drug for the treatment of intrahepatic tumor lesions.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L64 ANSWER 3 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 3

ACCESSION NUMBER: 2004:359113 HCAPLUS Full-text

DOCUMENT NUMBER: 142:85944

TITLE: Hyaluronic-acid butyric esters as promising antineoplastic agents in human lung carcinoma: A preclinical study

AUTHOR(S): **Coradini, Danila**; Pellizzaro, Cinzia; Abolafio, Gabriella; Bosco, Marco; Scarlata, Ignazio; Cantoni, Silvia; Stucchi, Luca; Zorzet, Sonia; Turrin, Claudia; Sava, Gianni; **Perbellini, Alberto**; Daidone, Maria Grazia

CORPORATE SOURCE: Unit of Biomolecular Determinants in Prognosis and Therapy, Experimental Department, Istituto Nazionale per lo Studio e la Cura dei Tumori, Milan, Neth.

SOURCE: Investigational New Drugs (2004), 22(3), 207-217
CODEN: INNDDK; ISSN: 0167-6997

PUBLISHER: Kluwer Academic Publishers

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 03 May 2004

AB New promising compds., derived from the esterification of hyaluronic acid with butyric acid, were investigated in vitro on a non-small cell lung carcinoma cell line (NCI-H460) and an its metastatic subclone (NCI-H460M). All new compds. exerted a dose-dependent inhibitory effect on both cell lines, which expressed CD44, the sp. surface receptor for hyaluronic acid, in a very high percentage of cells (90%). HE1, the most effective of these compds., was 10-fold more effective than sodium butyrate (NaB) in inhibiting cell proliferation. Similarly to NaB, after 24 h of treatment, HE1 affected the expression of three cell cycle-related proteins (p27kip1, p53 and p21waf1) responsible for growth arrest, indicating that the presence of the hyaluronic acid backbone does not interfere with the biol. activity. Intratumoral treatment with HE1 demonstrated a marked efficacy on primary tumor growth and on lung metastases formation of the murine Lewis Lung Carcinoma model.

Altogether, present findings suggest a possible clin. application of these novel butyric pro-drugs in primary and metastatic lung cancer.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L64 ANSWER 4 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 1999:246222 HCAPLUS Full-text
DOCUMENT NUMBER: 131:110966
TITLE: Hyaluronic acid as drug delivery for sodium butyrate: improvement of the anti-proliferative activity on a breast-cancer cell line
AUTHOR(S): **Coradini, Danila**; Pellizzaro, Cinzia; Miglierini, Giuliana; Daidone, Maria Grazia; **Perbellini, Alberto**
CORPORATE SOURCE: Oncologia Sperimentale C, Istituto Nazionale per lo Studio e la Cura dei Tumori, Milan, 20133, Italy
SOURCE: International Journal of Cancer (1999), 81(3), 411-416
CODEN: IJCNAW; ISSN: 0020-7136
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 22 Apr 1999
AB The potential clin. utility of sodium butyrate, a natural compound known to inhibit tumor-cell growth, is hampered by the difficulty of achieving effective in-vivo concns. The short half-life (about 5 min) of sodium butyrate results in rapid metabolism and excretion. To increase the availability of sodium butyrate over a longer period of time, we co-valently linked it to hyaluronic acid (a component of the extracellular matrix). Its major advantages as a drug carrier consist in its high biocompatibility and its ability to bind CD44, a specific membrane receptor frequently over-expressed on the tumor-cell surface. The degree of substitution of hyaluronic acid with butyrate residues ranged from d.s. = 0.10 to d.s. = 2.24 (1.8-28.4% weight/weight). The biol. activity of hyaluronic-acid-butyric-ester derivs. was evaluated in terms of the inhibition of the growth of the MCF7 cell line and compared with that of sodium butyrate. After 6 days of treatment, we observed a progressive improvement of the anti-proliferative activity up to d.s. = 0.20; thereafter, the anti-proliferative effect of the ester derivs. decreased. Fluorescence microscopy showed that after 2 h of treatment fluorescein-labeled compds. appeared to be almost completely internalized into MCF7 cells, expressing CD44 standard and variant isoforms. These findings indicate that hyaluronic acid could offer an important advantage in drug delivery, in addition to its biocompatibility: the ability to bind to CD44, which are known to be frequently over-expressed on the tumor-cell surface.
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L64 ANSWER 5 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1075830 HCAPLUS Full-text
DOCUMENT NUMBER: 143:360080
TITLE: Hyaluronic acid butyric esters with a low degree of substitution, procedure for their preparation, and their use in the treatment of cancer
INVENTOR(S): **Coradini, Danila**; **Perbellini, Alberto**
PATENT ASSIGNEE(S): **Sintofarm S.p.A., Italy**
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005092929	A1	20051006	WO 2005-IB780	20050325
WO 2005092929	A8	20060302		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1781707	A1	20070509	EP 2005-718276	20050325

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR

PRIORITY APPLN. INFO.: IT 2004-MI605 A 20040329
WO 2005-IB780 W 20050325

OTHER SOURCE(S): CASREACT 143:360080

ED Entered STN: 07 Oct 2005

AB The invention discloses hyaluronic acid butyric esters in which the hydroxyl groups of hyaluronic acid are partially esterified with butyric residues, characterized by a degree of substitution with butyric residues (ratio of number of butyric acid residues to disaccharide units GlcNAc-GlcUA of hyaluronic acid) being equal or below 0.1. These esters with low degree of substitution are obtained by means of a process carried out in the homogeneous phase under anhydrous conditions, wherein hyaluronic acid is used in the form of a quaternary nitrogen salt. The esters of the invention have a greater antiproliferative activity than corresponding esters with higher degree of substitution, and are particularly active against primary and metastatic tumors, where the tumors are primary of hepatic origin, or are hepatic metastases. A further aspect of the invention is represented by pharmaceutical compns., containing as active principle at least one of the esters described.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L64 ANSWER 6 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:610166 HCAPLUS Full-text
DOCUMENT NUMBER: 141:117165
TITLE: Use of retinoic esters of hyaluronic acid for the differentiation of totipotent stem cells
INVENTOR(S): **Perbellini, Alberto**; Ventura, Carlo; Maioli, Margherita
PATENT ASSIGNEE(S): **Sintofarm S.P.A., Italy**
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004063364	A1	20040729	WO 2004-EP183	20040114

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ

CA 2513337	A1	20040729	CA 2004-2513337	20040114
EP 1585811	A1	20051019	EP 2004-701903	20040114
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006515521	T	20060601	JP 2006-500559	20040114
US 2006216820	A1	20060928	US 2005-542302	20050714
PRIORITY APPLN. INFO.:			IT 2003-MI43 A	20030114
			WO 2004-EP183 W	20040114

ED Entered STN: 30 Jul 2004

AB The present invention relates to the use of hyaluronic esters of retinoic acid as stem cell pro-differentiation agents, in particular, to their ability to promote the appearance of a myocardial phenotype characterized by the presence of embryonic cardiomyocytes endowed with spontaneous contractile activity. The invention also relates to a process to differentiate said stem cells and to select mols. capable of modulating the pro-differentiating activity of these esters. The invention further relates to preparation of medicaments with a cardiogenic pro-differentiating activity for treatment and prevention of myocardial damages and of cardiomyopathies.

L64 ANSWER 7 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:546533 HCAPLUS Full-text
DOCUMENT NUMBER: 141:111540
TITLE: Mixed esters of hyaluronic acid with retinoic and butyric acids
INVENTOR(S): **Perbellini, Alberto; Coradini, Danila**
PATENT ASSIGNEE(S): **Sintofarm S.P.A., Italy**
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004056877	A1	20040708	WO 2003-EP14732	20031222
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2529816	A1	20040708	CA 2003-2529816	20031222
AU 2003294936	A1	20040714	AU 2003-294936	20031222
EP 1578803	A1	20050928	EP 2003-785916	20031222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2006074048	A1	20060406	US 2005-540939	20050623
PRIORITY APPLN. INFO.:			IT 2002-MI2745 A	20021223
			WO 2003-EP14732 W	20031222

ED Entered STN: 08 Jul 2004

AB The present invention relates to mixed esters of hyaluronic acid, wherein the hydroxyl groups are partially esterified with retinoic and butyric acids. These mixed esters are characterized by specific degrees of esterification and by a high ratio between the degree of substitution with butyric acid and retinoic acid. They exhibit a high anti-proliferative activity associated with activation of cell differentiation, with consequent clin. relevance in the treatment of hyper-proliferative pathologies and in particular of solid and systemic tumors.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L64 ANSWER 8 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:388548 HCAPLUS Full-text
DOCUMENT NUMBER: 129:67982
TITLE: Preparation of polysaccharide butyric esters as antitumors
INVENTOR(S): **Perbellini, Alberto; Coradini, Danila**
PATENT ASSIGNEE(S): Societa Cooperativa Centro Ricerche Poly-Tech A Responsabilita Limitata, Italy; Perbellini, Alberto; Coradini, Danila
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9823648	A1	19980604	WO 1997-EP6589	19971126
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2272720	A1	19980604	CA 1997-2272720	19971126
AU 9857515	A	19980622	AU 1998-57515	19971126
EP 941253	A1	19990915	EP 1997-953702	19971126
EP 941253	B1	20030528		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, FI				
JP 2001505940	T	20010508	JP 1998-524276	19971126
AT 241648	T	20030615	AT 1997-953702	19971126
US 6140313	A	20001031	US 1999-308832	19990525
PRIORITY APPLN. INFO.:			IT 1996-MI2505 A	19961129
			WO 1997-EP6589 W	19971126

ED Entered STN: 25 Jun 1998
AB The present application describes total or partial butyric esters of polysaccharides as novel compds.; the number of hydroxyl groups esterified with butyric residues per each glycosidic monomer is preferably higher than 0.001; the application also describes the process of preparation of said esters, their use in therapy as antiproliferative agents, and pharmaceutical compns. containing them. Thus, partially esterified hyaluronic acid with butyric anhydride is prepared and tested as antitumor agent.
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l64 9-11 ibib ab

L64 ANSWER 9 OF 11 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:483423 BIOSIS Full-text
DOCUMENT NUMBER: PREV200300483423
TITLE: 99mTc direct labelling and biodistribution studies on hyaluronan-butyrate, a promising antineoplastic agent.
AUTHOR(S): Rossin, R. [Reprint Author]; Zorzet, S.; Turrin, C.; Sava, G.; Giron, M. C.; Pellizzaro, C.; **Coradini, D.**; Scarlata, I.; Cantoni, S.; **Perbellini, A.**; Mazzi, U.
CORPORATE SOURCE: Dept. of Pharmaceutical Sciences, University of Padova, Via Marzolo 5, 35131, Padova, Italy
raffaella.rossin@unipd.it
SOURCE: Journal of Labelled Compounds and Radiopharmaceuticals, (August 2003) Vol. 46, No. Supplement 1, pp. S316. print.
Meeting Info.: 15th International Symposium on Radiopharmaceutical Chemistry. Sydney, Australia. August 10-14, 2003.
ISSN: 0362-4803 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 15 Oct 2003
Last Updated on STN: 15 Oct 2003

L64 ANSWER 10 OF 11 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 1998:194606 BIOSIS Full-text
DOCUMENT NUMBER: PREV199800194606
TITLE: Improvement of the antiproliferative activity of sodium butyrate by esterification with hyaluronic acid.
AUTHOR(S): **Coradini, D.** [Reprint author]; Pellizaro, C.; Khan, R.; Konowicz, P. A.; Miglierini, G.; Di Fronzo, G.; **Perbellini, A.**
CORPORATE SOURCE: Oncologia Sperimentale C, Istituto Nazionale per lo Studio Cura dei Tumori, Milano, Italy
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (March, 1998) Vol. 39, pp. 108. print.
Meeting Info.: 89th Annual Meeting of the American Association for Cancer Research. New Orleans, Louisiana, USA. March 28-April 1, 1998. American Association for Cancer Research.
ISSN: 0197-016X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 4 May 1998
Last Updated on STN: 4 May 1998

L64 ANSWER 11 OF 11 DRUGU COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-15079 DRUGU C P Full-text
TITLE: 99mTc Direct labelling and biodistribution studies on hyaluronan-butyrate, a promising antineoplastic agent.
AUTHOR: Rossin R; Zorzet S; Turrin S; Sava G; Giron M C; Pellizaro C; **Coradini D**; Scarlata I; Cantoni S; **Perbellini A**
CORPORATE SOURCE: Univ.Padua; Univ.Trieste; Nat.Inst.Cancer-Cure-Milan;

Sintofarm; Coimex
LOCATION: Milan, Padua, Trieste; Guastalla, It.
SOURCE: J.Labelled Compd.Radiopharm. (46, Suppl. 1, S316, 2003)
CODEN: JLCRD4 ISSN: 0022-2135
AVAIL. OF DOC.: Dept. of Pharmaceutical Sciences, University of Padova, via Marzolo 5, 35131 Padova, Italy. (11 Authors). (e-mail: raffaella.rossin@unipd.it).
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB The hyaluronate-butyrate conjugate (HA-But) shown previously to have enhanced antineoplastic activity compared to the unconjugated histone deacetylase inhibitor sodium butyrate, was radiolabeled with 99mTc by a direct method and evaluated for its in vitro uptake in 2 human hepatoma HepB3 and HepG2 cell lines and in vivo biodistribution There was a higher affinity for HepB3 than for HepG2 cells indicating a receptor-mediated endocytotic uptake. Biodistribution pattern depended on the route of administration: i.v. was the fastest route for delivery to the liver but i.p. or s.c. were preferred for a controled delivery to hepatic carcinomas. This confirmed that i.p. injected HA-But is a useful antineoplastic agent for treating primary or metastatic liver tumors. (conference abstract: 15th International Symposium on Radiopharmaceutical Chemistry, August 10-14, 2003, Sydney, Australia).

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=> d his nofile

     (FILE 'HOME' ENTERED AT 13:04:17 ON 17 MAY 2007)

     FILE 'HCAPLUS' ENTERED AT 13:04:35 ON 17 MAY 2007
               E US2005-540939/APPS
L1             1 SEA ABB=ON  PLU=ON  US2005-540939/AP
               D ALL

     FILE 'REGISTRY' ENTERED AT 13:05:38 ON 17 MAY 2007
L2             1 SEA ABB=ON  PLU=ON  HYALURONIC ACID/CN
               D RN
L3             1 SEA ABB=ON  PLU=ON  RETINOIC ACID/CN
               D RN
L4             1 SEA ABB=ON  PLU=ON  BUTYRIC ACID/CN
               D RN
L5             3 SEA ABB=ON  PLU=ON  (L2 OR L3 OR L4)

     FILE 'HCAPLUS' ENTERED AT 13:07:32 ON 17 MAY 2007
L6         52416 SEA ABB=ON  PLU=ON  L5
L7         18084 SEA ABB=ON  PLU=ON  9004-61-9/RN OR HYALURONIC ACID
L8         24095 SEA ABB=ON  PLU=ON  302-79-4/RN OR RETINOIC ACID

     FILE 'REGISTRY' ENTERED AT 13:10:15 ON 17 MAY 2007
L9             1 SEA ABB=ON  PLU=ON  107-92-6/RN

     FILE 'HCAPLUS' ENTERED AT 13:10:16 ON 17 MAY 2007
L10        22842 SEA ABB=ON  PLU=ON  L9
L11        51166 SEA ABB=ON  PLU=ON  107-92-6/RN OR BUTYRIC ACID
L12            5 SEA ABB=ON  PLU=ON  L7 AND L8 AND L11
L13          207 SEA ABB=ON  PLU=ON  L7 AND (L8 OR L11)
               E "MIXED ESTERS"/CT
L14        17563 SEA ABB=ON  PLU=ON  (MIX?) (2A) (ESTERIF? OR ESTER#)
L15            3 SEA ABB=ON  PLU=ON  L13 AND L14
               D SCAN
L16       897746 SEA ABB=ON  PLU=ON  ESTER# OR ESTERIF?
L17           61 SEA ABB=ON  PLU=ON  L13 AND L16
L18           61 SEA ABB=ON  PLU=ON  L15 OR L17
L19           55 SEA ABB=ON  PLU=ON  L18 (L) (THU OR PREP OR IMF OR SPN)/RL
               E "ANTITUMOR AGENTS"+PFT,OLD,NT/CT
L20       163865 SEA ABB=ON  PLU=ON  "ANTITUMOR AGENTS"/CT
L21           19 SEA ABB=ON  PLU=ON  L19 AND L20
L22         5231 SEA ABB=ON  PLU=ON  ESTER? (2A) PARTIAL?
L23            2 SEA ABB=ON  PLU=ON  L19 AND L22
L24      1424355 SEA ABB=ON  PLU=ON  1/SC,SX
L25           21 SEA ABB=ON  PLU=ON  L18 AND L24
L26           18 SEA ABB=ON  PLU=ON  L19 AND L24
L27           19 SEA ABB=ON  PLU=ON  L23 OR L26
               D KWIC 1-5

     FILE 'STNGUIDE' ENTERED AT 13:30:43 ON 17 MAY 2007

     FILE 'HCAPLUS' ENTERED AT 13:35:14 ON 17 MAY 2007
               D TI L27 1-19

     FILE 'STNGUIDE' ENTERED AT 13:35:14 ON 17 MAY 2007

     FILE 'HCAPLUS' ENTERED AT 13:36:26 ON 17 MAY 2007
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L28           0 SEA ABB=ON  PLU=ON  ALCOHOLATE (2A) HYALURONIC ACID
L29          33 SEA ABB=ON  PLU=ON  RETINOYL CHLORIDE
L30        1298 SEA ABB=ON  PLU=ON  BUTYRIC ANHYDRIDE
L31           1 SEA ABB=ON  PLU=ON  L13 AND (L29 OR L30)
                D TI
L32         665 SEA ABB=ON  PLU=ON  CELL? (2A) (HYPERPROLIF? OR HYPER(W)PROLIF?
                )
L33           0 SEA ABB=ON  PLU=ON  L13 AND L32
                SAVE TEMP L27 KRI439HCAP/A
                E PERBELLINI A?/AU
L34          17 SEA ABB=ON  PLU=ON  ("PERBELLINI A"/AU OR  "PERBELLINI
                ALBERTO"/AU)
                E CORADINI D?/AU
L35          46 SEA ABB=ON  PLU=ON  ("CORADINI D"/AU OR  "CORADINI DANILA"/AU)

L36           7 SEA ABB=ON  PLU=ON  L34 AND L35
L37          14 SEA ABB=ON  PLU=ON  L27 NOT L36
L38             QUE ABB=ON  PLU=ON  AY<2003 OR PY<2003 OR PRY<2003 OR MY<2003
                OR REVIEW/DT
L39           6 SEA ABB=ON  PLU=ON  L37 AND L38

     FILE 'MEDLINE, BIOSIS, DRUGU, BIOTECHNO, EMBASE' ENTERED AT 13:45:18 ON
     17 MAY 2007
L40       36886 SEA ABB=ON  PLU=ON  HYALURONIC ACID
L41       89306 SEA ABB=ON  PLU=ON  RETINOIC ACID
L42       36714 SEA ABB=ON  PLU=ON  BUTYRIC ACID
L43         258 SEA ABB=ON  PLU=ON  L40 AND (L41 OR L42)
L44        1492 SEA ABB=ON  PLU=ON  L14
L45         953 SEA ABB=ON  PLU=ON  L22
L46           2 SEA ABB=ON  PLU=ON  L43 AND (L44 OR L45)
L47      489675 SEA ABB=ON  PLU=ON  ESTER# OR ESTERIF?
L48          29 SEA ABB=ON  PLU=ON  L43 AND L47
                D KWIC 1-5
L49           8 SEA ABB=ON  PLU=ON  L48 AND L38
L50    16539283 SEA ABB=ON  PLU=ON  (PREPAR? OR PROCESS OR PROCESSES OR
                SYNTHE? OR METHOD? OR TECHNI?)
L51         171 SEA ABB=ON  PLU=ON  L43 AND L50
L52          11 SEA ABB=ON  PLU=ON  L47 AND L51
L53           1 SEA ABB=ON  PLU=ON  L52 AND L38
L54           8 SEA ABB=ON  PLU=ON  L49 OR L53
                D KWIC L52 1-5
L55         183 SEA ABB=ON  PLU=ON  PERBELLINI A?/AU
L56         301 SEA ABB=ON  PLU=ON  CORADINI D?/AU
L57          16 SEA ABB=ON  PLU=ON  L55 AND L56
L58          14 SEA ABB=ON  PLU=ON  L57 NOT L54
                SAVE TEMP L54 KRI439MULTI/A
                SAVE TEMP L58 KRI439MULAU/A

     FILE 'HCAPLUS' ENTERED AT 13:59:37 ON 17 MAY 2007
L59         159 SEA ABB=ON  PLU=ON  SINTOFARM?/CO,PA,CS
L60          56 SEA ABB=ON  PLU=ON  L34 OR L35
L61           3 SEA ABB=ON  PLU=ON  L59 AND L60
L62           8 SEA ABB=ON  PLU=ON  L61 OR L36

     FILE 'STNGUIDE' ENTERED AT 14:01:21 ON 17 MAY 2007
                D QUE L39
                D QUE L54

     FILE 'HCAPLUS, MEDLINE, BIOSIS, DRUGU, BIOTECHNO, EMBASE' ENTERED AT
     14:05:13 ON 17 MAY 2007
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L63          11 DUP REM L39 L54 (3 DUPLICATES REMOVED)
                ANSWERS '1-6' FROM FILE HCAPLUS
                ANSWER '7' FROM FILE MEDLINE
                ANSWER '8' FROM FILE BIOSIS
                ANSWERS '9-10' FROM FILE DRUGU
                ANSWER '11' FROM FILE BIOTECHNO
             D L63 1-6 IBIB ED ABS HITSTR HITIND
             D L63 7-11 IBIB AB HIT IND
             D QUE L62
             D QUE L58
L64          11 DUP REM L62 L58 (11 DUPLICATES REMOVED)
                ANSWERS '1-8' FROM FILE HCAPLUS
                ANSWERS '9-10' FROM FILE BIOSIS
                ANSWER '11' FROM FILE DRUGU
             D L64 1-8 IBIB ED ABS
             D L64 9-11 IBIB AB
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